OPEN PEER REVIEW

## Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

## What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

## Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
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- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://brieflands.com/briefland/knowledgebase/category/tree.html#opr.html

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# Peer Review Report for "Calcium Score of Iliac Vessels and Relative Sparing of the External Iliac Artery Could Recommend Surgical Arterial Graft Selection"

**Author(s):** Pooya Torkian, Taraneh Faghihi, Kobra Eslami, Abbas Arjmand Shabestari, Reza Talaie

## Review Timeline:

Submit Date: 8 Mar 2019
Revised Date: 3 Dec 2019
Accepted Date: 15 Dec 2019

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

**REFEREE**: Reviewer | Revision (0) 8 Apr 2019

Dear AE,
This is a retrospective study with evaluation of about 200 non contrast abdominopelvic CT scan in non selected patients for calcium scoring of arterial system.
- The study is very simple and descriptive with no valuable predictive relationship with this calcium scoring and outcome of vascular procedures.
- The subject is to show relative atherosclerotic sparing of the external iliac artery: and then one possibility
of a less vasculopathic arterial graft target .
- No significant clinical use could extract from this study.
- I think this manuscript could be more useful for vascular surgery journals .
- Some important notes are present which are ignored in this study:
1/In this study mean age of patients was 61.19
± 10.8 years but the mean age of renal transplantation usually is less than this age so the

result of this study could not distribute to these patients.
2/ In this study compare of calcium score between IIA and EIA was not present and this could be important for techniques of arterial anastomosis in renal transplantation.
3/In vascular bypass procedures EIA usually is not target site for anastomosis and usually bypass were done from abdominal aorta to femoral arteries so calcifications of EIA has importance .
4/Arterial wall Calcifications with or without atherosclerotic plaque and or luminal narrowing were indeterminate in this study .
5/No good patient selections was done for this subject because most patients were referred for urinary stone or infective collections.
Thanks.

**REFEREE**: Reviewer | **Revision** (0) 8 Apr 2019

Dear AE,
Hello, hope all are great and thank you so much for inviting me as a reviewer for this article, I appreciate a lot
Regarding this article, based on information provided, first of all, due to lack of novelty and secondly upon calcium scoring which is unable to exclude noncalcified plaque stenosis of vessels as External iliac artery, and thirdly well known agreement of using external iliac vessels for an organ transplant with no further need for investigation as this retrospective calcium score, in my opinion, this article does not have enough refreshing knowledge for publishing in this in the journal.
Thanks.

**REFEREE**: Reviewer | **Revision** (0) 10 Apr 2019

Dear AE,
Although the authors attempted to do a good quality study; but, there are some problems in statistical analysis, transparency, and clarity of method section and results in presentation; each of them is cited in detail, in the manuscript annexed file.
Thanks.

**REFEREE**: Reviewer | **Revision** (0) 11 Apr 2019

Dear AE,
Comments for the authors:
Title: Relative atherosclerotic sparing of the external iliac artery: possibility of a less vasculopathic arterial graft target
Thank you very much for sending the article for review. Here, the authors tried to test the hypothesis that whether external iliac artery (EIA) is less affected by atherosclerosis via measurement of Agatston score. Here are my comments:
1. The title should be revised. Here, the authors did not study the clinical outcome of arterial graft in the EIA. This needs a separate study and therefore, the title at least the part that EIA could be a better target for arterial graft should be removed. This can be recommended in the discussion part of the article and the fact that this requires further studies.
2. The data about confounding factors is missing. It is not clear what percentage of the

patients had conventional cardiovascular risk factors (smoking, dyslipidemia, etc).
3. I recommend a biostatistician review the article to place comments about the GEE (generalized estimating equation).
4. Who performed the measurement of Agatston score?
Thanks.

**REFEREE**: Associate Editor | **Revision (0)** 12 Apr 2019

Dear EIC,
The manuscript is studied, and there are some comments which should be addressed by the author. According to the comments, the document needs major revision.
Kind regards,

**REFEREE**: EIC | **Revision (0)** 13 Apr 2019

Dear authors,
Your article is not acceptable in this format and any decision depends on clearing the novelty of your study and revision according to the reviewer's comments.
If novelty can not be proved, the rest of the answers won't save the article.
Regards

OPEN PEER REVIEW

Revision (1)

## Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

It was a pleasure that our paper was reviewed by your journal editorial board. Here, you will find point-by-point reply to your comments: We re-edit the manuscript according to your expectations. Although the paper was edited by a native grammar checker, we try our best to re-edit it professionally to fulfill your requirement.

**Reviewer 1:**

Comments for statistical analysis and methods were put in the final portion of file.

**Reviewer 2:**

The aim of this study was to prove the hypothesis that the external iliac artery (EIA) shows significantly less calcified atherosclerosis in comparison with other adjacent arteries such as aorta, common iliac artery and common femoral artery. In our searches with broad spectrum of key words we did not find any documents or studies about sparing of EIA in calcified atherosclerotic process and in the same way there was no histologic justification for this incidence which it proves the novelty of our study. We found some histologic justifications for sparing of internal mammary artery from atherosclerotic process but there was no document about EIA.In some cases of obstruction in large arteries that cannot be recanalized by interventional procedures, synthetic grafts are used as a replacement for those occluded segment. Additionally, we know that in pulmonary atresia, synthetic grafts or xenografts are used as a conduit between RV and pulmonary artery beyond the atretic portion. One of the complications in these grafts is their calcification and occlusion. In so doing, in this study, we want to suggest a hypothesis by using harvested EIA from cadaver as grafts instead of those synthetic or xenografts. Although our recent study cannot predict that EIA will be a successful graft for this purpose but based on our data and clinical findings, it may have some histologic features in its wall which protects it from calcification, so trying it out can be worthwhile. For finding out these possible histologic features we want to start another study with our pathologist colleagues regarding full thickness EIA wall autopsy from cadavers and for permission of autopsy we needed the results of this recent study.

About the comparing of the mean age of our selected cases with the mean age of patients with renal transplantation, although our patients were older however it should be mentioned that we think about the whole life of patients after renal transplantation. We want to say that renal artery anastomosis to EIA may be safer than its anastomosis to IIA because of less possibility of future calcification in EIA. Because of proximity of IIA to pelvic bones, calculation of its calcification score had some technical problems and it is one of our study limitations.

Since CT scan was performed without administration of contrast we could not evaluate the luminal narrowing of studied arteries, however this finding was not the aim of our study and we only wanted to show less calcification of EIAs.

About patient selection, we include all patients who had been referred for non-contrast abdominopelvic CT scan for any reason. These include patients with suspicion for renal stone or patients who had any contraindication for contrast administration such as renal failure or sensitivity to contrast. Forcing other patients without indication for non-contrast abdominopelvic CT scan would not be ethical, so this was our solely option.

**Reviewer 3:**

We do agree with your suggestion and the title was corrected. We corrected the title of our manuscript to “Relative calcified atherosclerotic sparing of the external iliac artery: suggesting its usage as an arterial graft”

Unfortunately, we did not have access to some patient’s data about their atherosclerotic risk factors and it was one of our study limitations however since we compare different arteries with each other in each patient and not between different patients it may have less confounding effects.

The Agatston score measurement was performed by a radiologist using a software on Philips workstation for calculating the calcium score.

Comments about statistical point of view was placed in the final portion of file.

**Reviewer 4:**

The aim of this study was to prove the hypothesis that the external iliac artery (EIA) shows significantly less calcified atherosclerosis in comparison with other adjacent arteries such as aorta, common iliac artery and common femoral artery. In our searches with broad spectrum of key words we did not find any documents or studies about sparing of EIA in calcified atherosclerotic process and in the same way there was no histologic justification for this incidence which it proves the novelty of our study. We found some histologic justifications for sparing of internal mammary artery from atherosclerotic process but there was no document about EIA.In some cases of obstruction in large arteries that cannot be recanalized by interventional procedures, synthetic grafts are used as a replacement for those occluded segment. Additionally, we know that in pulmonary atresia, synthetic grafts or xenografts are used as a conduit between RV and pulmonary artery beyond the atretic portion. One of the complications in these grafts is their calcification and occlusion. In so doing, in this study, we want to suggest a hypothesis by using harvested EIA from cadaver as grafts instead of those synthetic or xenografts. Although our recent study cannot predict that EIA will be a successful graft for this purpose but based on our data and clinical findings, it may have some histologic features in its wall which protects it from calcification, so trying it out can be worthwhile. For finding out these possible histologic features we want to start another study with our pathologist colleagues

regarding full thickness EIA wall autopsy from cadavers and for permission of autopsy we needed the results of this recent study.

About the comparing of the mean age of our selected cases with the mean age of patients with renal transplantation, although our patients were older however it should be mentioned that we think about the whole life of patients after renal transplantation. We want to say that renal artery anastomosis to EIA may be safer than its anastomosis to IIA because of less possibility of future calcification in EIA. Because of proximity of IIA to pelvic bones, calculation of its calcification score had some technical problems and it is one of our study limitations.

**Point- by – point reply for Statistical point of view comments:**

1. The reason for using this model was:
Each subject was measured several times according to his/her artery type and these structure of the data was correlated for every patient.
The outcome of data was considered as an ordinal one and reaching higher level of calcium was our goal.
Factoring in these two items, we used GEE method and cumulative ordinal link function to evaluate the calcification level in different arteries and compare the different calcification level of arteries.

2. The effects of age, gender, Smoking status, Hypertension, Diabetes and Hyperlipidemia were adjusted in GEE model . Unfortunately, we did not have access to some patient’s data about their atherosclerotic risk factors and it was one of our study limitations however since we compare different arteries with each other in each patient and not between different patients it may have less confounding effects.

3. The reason for using this model was:
Each subject was measured several times according to his/her artery type and these structure of the data was correlated for every patient.
The outcome of data was considered as an ordinal one and reaching higher level of calcium was our goal.

Factoring in these two items, we used GEE method and cumulative ordinal link function to evaluate the calcification level in different arteries and compare the different calcification level of arteries.

4. Cumulative logistic has the same function to ordinal logistic for correlated data. we replace term with:
cumulative ordinal with logistic function

5. In this study we performed univariate analysis to evaluate the different arteries based on different calcification levels using GEE.
GEE was conducted for high and low level Aorta calcification to test the associations in two groups separately. So, there were same results in two mentioned stratified groups.

**Comments for Table:**

1. The average calcification score was the lowest in the right EIA segment (18.21), which was selected as the reference group

2. p-values were deleted from this table.

3. Because we dont want to reiterate the same results we just put data based on this analysis in table 2 so we suffice to this table.

**OPEN PEER REVIEW**

**Revision (1)**

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

**REFEREE**: Reviewer | **Revision** (1) 20 May 2019

Dear AE,
Unfortunately, despite the explanation and some changes in the article, these are not convincing, and some cases were ignored.
Thanks.

**REFEREE**: Reviewer | **Revision** (1) 24 May 2019

Dear AE,
Title: Relative calcified atherosclerotic sparing of the external iliac artery: suggesting its usage as an arterial graft
Comments for the authros:
1. The title has been changed. However, as this has been mentioned by another reviewer, the external iliac artery is already used as an arterial graft in some procedures. So, suggesting it as an arterial graft could not be a good title. Also, as stated below the population studied does not reflect the population who needs artery graft or anastomosis. So, suggesting EIA as a target for arterial graft in the title is not appropriate.
2. Please define abbreviations in the abstract: EIA (external iliac artery)
3. The manuscript still needs some edit. For example, the abstract: “the Odds ratio (OR) of the left EIA for reaching a higher calcium score level was 1.19 (P=0.44, not significant)” “odds” should not be in capital letter. There is no need to add “not significant” beside a P value of 0.44.
4. Abstract: “Objective: The purpose of this study was to assess the degree of atherosclerotic calcification in pelvic vessels.”
It could be revised as “To assess atherosclerotic calcification of the pelvic vessels via measuring Agatston score and compare it among the abdominal aorta, external iliac artery (EIA), common iliac artery (CIA), and common femoral artery (CFA).”
5. The keywords should be revised considering MeSH services a useful guide for selecting them:
I think the MeSH terms “atherosclerosis” and “arteries” should have a place in the list.
6. Methods section: The inclusion criteria for unenhanced CT scans are: Patients with non-traumatic abdominal pain, suspected renal stones, urologic disorders or fever of unknown origin (highly suspected to be of abdominal abscess).
These are the patients who were not candidate for arterial graft and their CT scan and calcifications were measured. Therefore, the results of these apparently not severely

affected subjects (I mean no chronic disease similar to those who are at the end stage of vascular disease or renal failure who need renal replacement who require arterial anastomosis) may not be generalizable to patients in real practice who need arterial graft and therefore may have different calcification scores (i.e., Agatston score).
This is the reason that the topic of arterial graft should not be bold in this manuscript. It should be removed from the title and conclusion of the manuscript. The better form is to suggest further studies in renal transplantation candidates with Agatston score to find out whether such lower Agatston score still is detected in renal transplant candidates or not.
7. Figure 3 has very low resolution. This should be substituted with a better quality image.
8. Figure 2 has also low resolution.
Thanks.

**REFEREE**: Associate Editor | **Revision (1)** 31 May 2019

Dear EIC,
The manuscript is studied, and there are some comments which should be addressed by the author. According to the comments, the document needs major revision.
Kind regards,

**REFEREE**: EIC | **Revision (1)** 1 Jun 2019

Dear Author,
The reviewers' comments are mentioned. Please correct the details as mentioned above carefully according to reviewers' request.
Thanks.

OPEN PEER REVIEW

Revision (2)

## Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Thanks for your comments. Here, you will find point-by-point reply to your comments:

1. We revised it.
2. In our study, we used non-contrast CT, so we couldn't detect non-calcified plaque. However, in our future study we are going to collect data from non-calcified plaque involvement of EIA.
3. Due to close proximity of IIA to sacral bone and calcificaition in its small branches, we couldn't measure its calcium score by our software meticulously.
4. Since EIA has not been used as a conduit for connecting RV to pulmonary artery in patients with pulmonary atresia, we suggest EIA as a conduit for RV to pulmonary artery connection. Although our included patients didn't require graft, the result of study demonstrated that EIA can be a good graft option for candidates.
5. Corrected
6. Corrected
7. Corrected
8. Corrected
9. Some patients in our study had renal failure and we didn't exclude them. In our analysis, patients with Renal failure has been included and we calculated the atherosclerotic calcification of their pelvic vessels. Hence, we aim to include patients solely with renal failure in our next future study.
10. Some patients in our study had renal failure and we didn't exclude them. In our analysis, patients with Renal failure has been included and we calculated the atherosclerotic calcification of their pelvic vessels. Hence, we aim to include patients solely with renal failure in our next future study.

11. Corrected
12. Corrected

Thanks

**OPEN PEER REVIEW**

**Revision (2)**

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

**REFEREE**: Associate Editor | **Revision** (2) 16 Jul 2019

Dear EIC
The reviewer(s) have recommended publication, but also suggest some minor revisions to the manuscript. Therefore, I invite the author to respond to the reviewer(s)' comments and revise his manuscript.
Kind regards,

**REFEREE**: EIC | **Revision** (2) 17 Jul 2019

Dear Author,
Your article is reviewed by the reviewers carefully. According to their comments, this document needs minor revision. Please follow their comments as requested.
Thanks.

OPEN PEER REVIEW

Revision (3)

## Reply to Reviewers

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You can read the authors' responses to the reviewers' comments in the next page.

Thanks for your comments. Here, you will find point-by-point reply to your comments:

1. The pdf file was rechecked and the manuscript was checked and proof-read by a native English editor.
2. The title was changed based on your suggestion.
3. Added
4. Added

Thanks

**OPEN PEER REVIEW**

**Revision (3)**

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

**REFEREE**: EIC | **Revision** (3) 31 Aug 2019

Dear Author,
Your article is reviewed by the reviewers carefully. According to their comments, this document needs minor revision. Please follow their comments as requested.
Thanks.

OPEN PEER REVIEW

Revision (4)

## Reply to Reviewers

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You can read the authors' responses to the reviewers' comments in the next page.

Thanks for your comments. Here, you will find point-by-point reply to your comments:

1. The pdf file was rechecked and the manuscript was checked and proof-read by a native English editor.

Thanks

**OPEN PEER REVIEW**

**Revision (4)**

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

**Marzieh Motevalli**: Associate Editor | **Revision** (4) 19 Oct 2019

Dear EIC
Based on the authors' answers to the reviewers' comments, the reviewer(s) have recommended publication.
Kind regards.

**Mehranoosh Dolatshahi**: Associate Editor | **Revision** (4) 30 Nov 2019

Dear EIC
The reviewer(s) have recommended publication, but also suggest some minor revisions to the manuscript. Therefore, I invite the author to respond to the reviewer(s)' comments and revise his manuscript.
Kind regards,

**Kavous Firouznia**: EIC | **Revision** (4) 30 Nov 2019

Dear authors,
Your article needs Minor Revision.
Regards

OPEN PEER REVIEW

Revision (5)

## Reply to Reviewers

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You can read the authors' responses to the reviewers' comments in the next page.

Thanks for your comments. Here, you will find point-by-point reply to your comments:

1)Corrected.

2)Corrected.

3) New and high resolution figures were added. Unfortunately, uploaded figures had been changed to low-resolution ones while we uploaded them to the journal site. We would appreciate it to guide us through different ways in order to send the original items ( email,....) .

Thanks

OPEN PEER REVIEW

Revision (5)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

**Mehranoosh Dolatshahi**: Associate Editor | **Revision** (5) 14 Dec 2019

Dear EIC
Based on the authors' answers to the reviewers' comments, the reviewer(s) have recommended publication.
Kind regards.

**Kavous Firouznia**: EIC | **Revision** (5) 15 Dec 2019

Dear authors,
Your article is acceptable for the publication.
Regards